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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/701,236	BAKER ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,69 and 71-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,69 and 71-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/20/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Double Patenting

Claims 1, 69 and 71-77 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 8, 19-22, 54, 57 and 63 of copending Application No. 10/700,697. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '697 application are directed to modified duplex RNAs comprising 2'-substitutions, which are a species that anticipates the claims of the instant application, which are directed generically to duplex RNAs comprising sugar surrogates. The term sugar surrogate is not explicitly defined in the instant specification, but is described only by exemplification. Contemplated sugar surrogates include arabino nucleotides, pyrrolidine nucleotides and 4'-thioribose nucleotides. In view of the lack of an explicit definition for the term sugar surrogate, this term is interpreted as any entity other than the naturally occurring ribose nucleoside that is capable of use in an oligonucleotide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 69 and 71-77 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,7-9,16,18-22,26-

31,73 and 76-85 of copending Application No. 10/701,264. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '264 application are directed to modified duplex RNAs comprising 2'-OMe substitutions, which are a species that anticipates the claims of the instant application, which are directed generically to duplex RNAs comprising sugar surrogates. The term sugar surrogate is not explicitly defined in the instant specification, but is described only by exemplification. Contemplated sugar surrogates include arabino nucleotides, pyrrolidine nucleotides and 4'-thioribose nucleotides. In view of the lack of an explicit definition for the term sugar surrogate, this term is interpreted as any entity other than the naturally occurring ribose nucleoside that is capable of use in an oligonucleotide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 69 and 71-77 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 9, 11, 75, 78 and 93-97 of copending Application No. 10/701,316. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '316 application are directed to modified duplex RNAs comprising 2'-substitutions, which are a species that anticipates the claims of the instant application, which are directed generically to duplex RNAs comprising sugar surrogates. The term sugar surrogate is not explicitly defined in the instant specification, but is described only by exemplification. Contemplated sugar surrogates include arabino nucleotides, pyrrolidine nucleotides and 4'-thioribose nucleotides. In view of the lack of an explicit definition for the term sugar

surrogate, this term is interpreted as any entity other than the naturally occurring ribose nucleoside that is capable of use in an oligonucleotide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments: Double Patenting

Applicants' request that the provisional double patenting rejections be held in abeyance until claims are found allowable is acknowledged, but until the rejections have been overcome, it is proper to maintain the rejections.

Claim Objections

Applicant is advised that should claim 69 be found allowable, claim 74 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof because the text of claim 74 is identical to claim 69. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

Claims 1, 69 and 74-76 are rejected under 35 U.S.C. 102(a) as being anticipated by Bevilacqua et al. (Biochemistry 1996, of record).

The claims are directed to compositions comprising chemically synthesized oligomers that comprise about 12 to about 30 nucleotides, are not covalently linked and

are at least partially complementary to each other; at least one strand is partially complementary to a target nucleic acid. Each strand comprises at least one sugar surrogate and at least one strand has a plurality of 2'-hydroxy-pentofuranosyl sugar moieties. In specific embodiments the ribonucleotides are in the second oligomer, the oligomers are chimeric oligonucleotides that may be gapmers or hemimers, are formulated with a pharmaceutically acceptable carrier, are complementary over at least 17 contiguous nucleotides or are about 15 to about 25 nucleotides in length.

Bevilacqua et al. disclose (see figure 5 and description on page 9988, first column) chimeric dsRNA duplexes that correspond to the 22 nucleotides of the TAR gene. Each strand contains areas of 2'-OMe substitutions and ribonucleotides, making chimeric oligonucleotides comprising two regions of nucleosides of two different types. Gapmers, 5'-hemimers and 3'-hemimers are defined as having one or more terminal segments with nucleosides of a first type and a further segment with nucleosides of a second type. The use of the open language "comprising" in the definition of the chimeric oligonucleotides allows for the presence of additional regions, therefore the dsRNAs meet the limitations of claims 21, 22 and 26-31. This duplex is used in to probe the sequence recognition of the enzyme PKR, which involves formulation of the duplex as a composition with a pharmaceutically acceptable carrier.

Thus, Bevilacqua et al. disclose all limitations of and anticipate claims 1, 69 and 74-76.

Response to Arguments

Applicants traverse the rejection over Bevilacqua by arguing that the modified sequence in Bevilacqua is not 100% complementary to a target mRNA, noting that TAR is not a "target mRNA" as recited in the present claims but is an untranslated regulatory sequence of HIV RNA. this argument is not persuasive because the instant specification defines the targeted sequences broadly as encompassing any nucleic acid capable of being targeted, therefore even though TAR is an untranslated sequence it nevertheless meets the definition of a target mRNA.

Applicants additionally argue that the modified duplexes discussed in Figure 5 and on page 9988 are not even complementary to TAR, noting that the experiments described in figure 5 were designed to assess the "sequence independent recognition by a protein". This argument is not persuasive because the page pointed to by applicants as evidence that the experiments assessed sequence independent recognition by a protein actually states that there are two positions within dsRNA that are accessible for sequence-independent recognition by a protein, not that the experiments were done using non-TAR sequences.

Claims 1, 69 and 74-76 are rejected under 35 U.S.C. 102(a) as being anticipated by Yu et al. (RNA 1997).

The claims are directed to compositions comprising chemically synthesized oligomers that comprise about 12 to about 30 nucleotides, are not covalently linked and are at least partially complementary to each other; at least one strand is partially complementary to a target nucleic acid. Each strand comprises at least one sugar

surrogate and at least one strand has a plurality of 2'-hydroxy-pentofuranosyl sugar moieties. In specific embodiments the ribonucleotides are in the second oligomer, the oligomers are chimeric oligonucleotides that may be gapmers or hemimers, are formulated with a pharmaceutically acceptable carrier, are complementary over at least 17 contiguous nucleotides or are about 15 to about 25 nucleotides in length.

Yu et al. disclose in figure 1C a duplex comprising one strand of RNA corresponding to a 24-nucleotide portion of 28S ribosomal RNA with one 2'-OMe substitution. The other strand of the duplex is 18 nucleotides in length and comprises a chimeric gapmer oligonucleotide of 2'-OMe and 2'-deoxy nucleotides. 5'-hemimers and 3'-hemimers are defined (see claims 27 and 30) as having a terminal segment with nucleosides of a first type and a further segment with nucleosides of a second type. The use of the open language "comprising" in the definition of the hemimer allows for the presence of additional regions, therefore the gapmer molecule meets the limitations of claims 26-31. This duplex is used in an RNase H cleavage assay, which involves formulation of the duplex as a composition with a pharmaceutically acceptable carrier.

Thus, Yu et al. disclose all limitations of and anticipate claims 1, 69 and 74-76.

Response to Arguments

Applicants traverse the rejection over Yu et al. by arguing that the modified sequence in Yu is not 100% complementary to a target mRNA, noting that the modified duplexes in Yu correspond to a portion of 28S ribosomal RNA. This is not persuasive because as described in response to the previous arguments, the specification broadly defines targets as encompassing any nucleic acid capable of being targeted.

Claim Rejections - 35 USC § 103

Claims 1, 69 and 71-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. as applied to claims 1, 69 and 74-76 above, and further in view of Stec et al. (US 5,151,510, of record) and Summerton et al. (US 5,142,047).

Claims 1, 69 and 74-76 are described in the 102 rejection over Yu et al. Claims 71 and 72 recite that one or both of the oligomeric compounds of the composition have at least one phosphorothioate linkage. Claim 73 recites the presence of particular sugar surrogates and claim 77 recites that the oligomeric compound comprises at least two modified nucleosides.

Yu et al. disclose a duplex RNA comprising 2'-OMe substitution and a plurality of ribonucleotides as described fully in the 102 rejection over this reference. Yu et al. do not teach their duplex as containing phosphorothioate linkages and do not teach the use of other sugar surrogates.

It was well known in the art at the time the invention was made to incorporate modified nucleotides, including phosphorothioate linkages and modified sugars such as morpholino sugars, into an oligonucleotide for the purpose of increasing stability and nuclease resistance. See for example, Stec et al. who teach the use of phosphorothioate linkages for these desirable properties and Summerton et al., who teach morpholino sugar groups that can be incorporated into oligonucleotides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce the duplex taught by Yu et al. as useful in RNase H cleavage assays and to modify these duplexes with modified nucleotides such as

phosphorothioate linkages or morpholino sugars in order to determine if these modifications will provide active substrates for RNase H. One of ordinary skill in the art would have had a motivation and reasonable expectation of success in doing so based on the recognition in the art that use of modified nucleotides such as phosphorothioate linkages and morpholino sugars provide the advantages of increased stability and nuclease resistance.

Thus, the invention of claims 1, 69 and 71-77 would have been obvious, as a whole, at the time the invention was made.

Response to Arguments

Applicants traverse the 103 rejection by arguing that Yu et al. do not teach a sequence complementary to mRNA, this argument has been addressed above. Applicants further argue that no reason has been provided why one would modify the duplex taught by Yu et al. This argument is not persuasive because Yu et al. teach that their duplex is useful in RNase H cleavage assays, therefore one would incorporate modified nucleotides in order to test the modified duplexes for such activity.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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